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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,120	07/14/2005	Kaw Yan Chua	11747.105002 NUS002	2575

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
11/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,120	CHUA ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-15,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/17/2005 & 11/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group XI, claims 16-27 and the species of SEQ ID NO:5 and intramuscular administration in the reply filed on 02/15/2008 is acknowledged.

2. Claims 1-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group and claims 21-22 are withdrawn as being directed to a non-elected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/15/2008.

3. Claims 16-20 and 23-27 are currently under examination as they read on a method for immunization against an allergen comprising administering to a subject the recombinant nucleic acid of SEQ ID NO:5 and Der p I to the subject by intramuscular administration.

4. Applicant's IDS documents filed on 11/16/2006 & 10/17/2005 are acknowledged.

Claim Objections

5. Claims 16 and 25 are objected to because of the following informalities: Claims 16 and 25 are dependent upon non-elected base claims 1-13. Appropriate correction is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 16-20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year; does not reasonably provide enablement for: a method for immunization against an allergen comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum, wherein the **first signal peptide** is the **N- terminal signal peptide of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-seleetin, tyrosinase, GLUT4, endotubin or Nefprotein or a functional equivalent thereof**; further comprising **an operably linked gene encoding a targeting peptide** wherein **targeting peptide** targets **the allergen** to an endosome or lysosome; wherein the **targeting peptide** is the **C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef protein or a functional equivalent thereof**; wherein **the targeting peptide** is the **transmembrane and cytoplasmic domain.of LAMP-1**; or **which encodes the allergen a T helper cell epitope thereof, or a antigenic fragment thereof containing one or more T helper cell epitope or a**

functional equivalent and in a second phase administering **the allergen** to the subject; or a method for treating or **preventing** an allergic reaction in a subject comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum, wherein the **first signal peptide** is the **N- terminal signal peptide of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-seleetin, tyrosinase, GLUT4, endotubin or Nefprotein or a functional equivalent thereof**; further comprising **an operably linked gene encoding a targeting peptide** wherein **targeting peptide** targets **the allergen** to an endosome or lysosome; wherein the **targeting peptide** is the **C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef protein or a functional equivalent thereof**; wherein **the targeting peptide** is the **transmembrane and cytoplasmic domain.of LAMP-1**; or **which encodes the allergen a T helper cell epitope thereof, or a antigenic fragment thereof containing one or more T helper cell epitope or a functional equivalent** and in a second phase administering **the allergen** to the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year.

The instant claimed reads on the administration all whole allergens, T helper cell epitopes thereof, antigenic fragment thereof containing one or more T helper cell epitopes, functional equivalents thereof and all recombinant nucleic acids encoding the genus of all aforementioned allergens. First, the structures of all allergens are not known therefore the instant claim recitations encompass allergens presently unidentified by scientists. Further, the term

"functional equivalents thereof" encompasses any of the recited allergen sequences having any number of undisclosed additions, deletions and/or substitutions, including functional equivalents whose function is due to undisclosed parts of the molecule irrespective of the allergen sequence. Predicting what allergens and derivatives thereof can be used in the instant invention is unpredictable. Since the specification fails to provide guidance regarding which allergens sequences other than the Der p I sequence of instant SEQ ID NO:5 and the native Der p I protein can work in the claimed invention it follows that any other allergens are not enabled. It was well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds could result in substantially different pharmacological activities. For example, the relationship between the sequence of a protein and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (Ngo et al., PTO-892, Reference U). Blumenthal et al. teaches that correlations between structure and IgE binding (or the lack of IgE binding) cannot be predicted on an a priori structural basis (PTO-892, Reference V, see entire document and page 39 of third full paragraph). Skolnick et al. teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure, i.e., amino acid sequence, does not necessary tell one its function (PTO-892, Reference W, entire document and abstract). Attwood et al. teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (PTO-892, Reference X, entire document). Because of the diversity of B cell epitopes ranging from conformational to linear epitope structures, there is no predictability regarding what effect amino acid substitutions, deletions and additions will have on the structure and

function of all allergens because it is difficult to predict the 3-D structure of modified allergens from a primary structure such as amino acid sequence alignment. Given the lack of guidance as to which specific amino acids within the any known or unknown allergens can tolerate change, it is unpredictable which whole allergens, T helper cell epitopes thereof, antigenic fragment thereof containing one or more T helper cell epitopes, functional equivalents thereof and all recombinant nucleic acids encoding the genus of all aforementioned allergens including those presently unidentified by scientists could be used to practice the instant invention commensurate in scope with the claims.

The specification has not adequately disclosed the genus of all "signal" and "targetting" peptides for use in the claimed invention. Without a specific, limiting definition in the specification, these terms encompass the genus of all peptides. The specification has not adequately disclosed the genus of all signal and targeting peptides for use in the claimed invention. One of ordinary skill in the art would be required to practice undue experimentation to practice the claimed invention commensurate in scope with the claims.

The instant claims also recite the N- terminal signal peptides of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin and Nef , the C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef ; and the transmembrane and cytoplasmic domain of LAMP-1 or a functional equivalents thereof. For the same reasons as state above with reference to the allergen and nucleic acids encoding

allergens, the specification does not adequately disclose the genus of all N- terminal signal peptides of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin and Nef , the C- terminal lysosome or endosome targeting sequences of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef ; and the transmembrane and cytoplasmic domains of LAMP-1 or a functional equivalents thereof. The specification only discloses immunization with the *Mus musculus* N-terminal signal peptide of LAMP-1, the entire Der p I gene product and the *Mus musculus* transmembrant and cytoplasmic domain of SEQ ID NO:5. The term "functional equivalents thereof" encompasses any of the recited signal peptide sequences having any number of undisclosed additions, deletions and/or substitutions, including functional equivalents whose function is due to undisclosed parts of the molecule irrespective of the recited signal peptides. Further, without reference to the sequences encompassed by the terms N- terminal signal peptide of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin and Nef , the C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef ; and the transmembrane and cytoplasmic domain of LAMP-1, one of ordinary skill in the art would be required to perform undue experimentation to determine which amino acid sequences are meant to be encompassed by the instant laboratory designations.

Further at issue is whether or not the claimed method would function to "prevent" allergy. The specification provides no in vivo data to support the claimed subject matter. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy

using any recited composition. The invention may evaluate compounds which reduce the likelihood of an allergy by administering the compound, but the specification does not disclose how to totally prevent allergy. Therefore, the specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of allergy by administering the claimed compositions.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 16-20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and wherein

multiple doses of the nucleic acid is administered in the first phase over a period of about a year.

Applicant is not in possession of: a method for immunization against an allergen comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum, wherein the **first signal peptide** is the **N- terminal signal peptide of LAMP-I, human tissue plasminogen activator, LAMP-II, DEC-205, P-seleetin, tyrosinase, GLUT4, endotubin or Nefprotein or a functional equivalent thereof**; further comprising **an operably linked gene encoding a targeting peptide** wherein **targeting peptide** targets **the allergen** to an endosome or lysosome; wherein the **targeting peptide** is the **C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef protein or a functional equivalent thereof**; wherein **the targeting peptide** is the **transmembrane and cytoplasmic domain.of LAMP-1**; or **which encodes the allergen a T helper cell epitope thereof, or a antigenic fragment thereof containing one or more T helper cell epitope or a functional equivalent** and in a second phase administering **the allergen** to the subject; or a method for treating or preventing an allergic reaction in a subject comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum, wherein the **first signal peptide** is the **N- terminal signal peptide of LAMP-I, human tissue plasminogen activator, LAMP-II,**

DEC-205, P-seleetin, tyrosinase, GLUT4, endotubin or Nefprotein or a functional equivalent thereof; further comprising **an operably linked gene encoding a targeting peptide** wherein **targeting peptide** targets **the allergen** to an endosome or lysosome; wherein the **targeting peptide** is the **C- terminal lysosome or endosome targeting sequence of LAMP-1, human tissue plasminogen activator, LAMP-II, DEC-205, P-selectin, tyrosinase, GLUT4, endotubin or Nef protein or a functional equivalent thereof**; wherein **the targeting peptide** is the **transmembrane and cytoplasmic domain.of LAMP-1**; or **which encodes the allergen a T helper cell epitope thereof, or a antigenic fragment thereof containing one or more T helper cell epitope or a functional equivalent** and in a second phase administering **the allergen** to the subject.

The specification discloses a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant. Other than the specific recombinant nucleic acid of SEQ ID NO:5 and Der p I allergen, there is inadequate written description of the structure and functions for any other recombinant nucleic acids and allergens as set forth in the claims.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be

satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 24, 2008

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Maher M. Haddad/

Primary Examiner, Art Unit 1644